

# MOLECULAR BIOLOGY AND BIOTECHNOLOGY

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A Comprehensive Desk Reference

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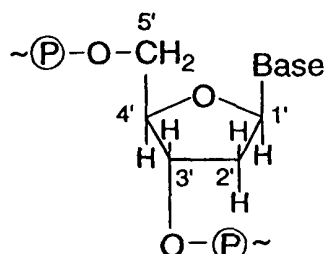
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somewhat over strand breakage. A number of altered sugars are related to these processes have been identified, both in the presence and in the presence of oxygen. Based on detailed model studies, the reactions and their kinetics leading to strand breakage in the absence of oxygen are fairly well understood. The primary mechanism is the abstraction of the H atom at C-4':



This radical then eliminates a neighboring phosphate (linked to a segment of the DNA strand), leaving behind a radical cation that can react with water, either at the position that has eliminated the phosphate, or at C-4'. In the former case the other phosphate group may be eliminated by the same mechanism; in double-stranded DNA this sequence of events produces a clean gap in the affected strand (the end groups of the two fragments are phosphate groups), with the loss of some information because of the disappearance of the damaged nucleoside. In the latter case the base is also lost, but additionally at the end of one of the fragment strands a damaged sugar remains linked to the phosphate group—enzymatically speaking, it is a “dirty” end group. Details of the mechanism of DNA strand breakage under conditions of oxygenation are less well understood, but some of the relevant sugar lesions have been detected. Model systems (ribose 5-phosphate) indicate that under these conditions C-5' should be an additional site of attack and, by analogy, one would expect (no experimental evidence yet) the 5'-peroxyl radical also to be a potential precursor for strand breakage.

So far, sugar damage has been discussed only in terms of OH radicals attacking this moiety. A contribution of the direct effect of ionization of the sugar moiety and the phosphate groups) must also be considered, but experimental evidence is not yet available. However, there is another interesting aspect. In polynucleotides such as poly(U) and poly(C), there is convincing evidence that base radicals are the major precursors of the sugar radicals that lead to strand breakage and the release of an unmodified base at the site of the damaged sugar. It is less clear whether such a radical transfer from the base to the sugar moiety can also occur in DNA. In mammalian cells, DNA double-strand breaks are observed alongside single-strand breaks approximately in the ratio of 1 : 25. This poses the question of how these double-strand breaks are formed. It has been argued here that they result from clustered lesions. In the literature, an additional one-hit route has been suggested that involves a radical transfer from the already broken strand to the sugar moiety of the opposite strand, followed by breakage of this strand.

Carbon-centered radicals are known to add to the C=C bonds of nucleobases. Such reactions, as well as radical-radical combination reactions involving macroradicals, in principle allow the formation of DNA-protein and DNA-DNA cross-links. In special cases, such products have been observed with biological material, albeit in yields considerably lower than DNA double-strand breaks.

See also DNA DAMAGE AND REPAIR; FREE RADICALS IN BIOCHEMISTRY AND MEDICINE; ULTRAVIOLET RADIATION DAMAGE TO DNA.

### Bibliography

- Dizdaroglu, M. (1991) *Free Radical Biol. Med.* 10:225.  
 Hüttermann, J. (1991) In *Radical Ionic Systems*, A. Lund, and M. Shiotani, Eds., p. 435. Kluwer, Dordrecht.  
 Michael, B. D., Held, K. D., and Harrop, H. A. (1983) In *Radioprotectors and Anticarcinogens*, O. Nygaard and M. G. Simic, Eds., p. 325. Academic Press, New York.  
 Schulte-Frohlinde, D., Simic, M. G., and Görner, H. (1990) *Photochem. Photobiol.* 52:1137.  
 Steenken, S. (1989) *Chem. Rev.* 89:503.  
 Teebor, G. W., Boorstein, R. J., and Cadet, J. (1988) *Int. J. Radiat. Biol.* 54:131.  
 von Sonntag, C. (1987) *The Chemical Basis of Radiation Biology*. Taylor & Francis, London.  
 von Sonntag, C., Hagen, U., Schön-Bopp, A., and Schulte-Frohlinde, D. (1981) *Adv. Radiat. Biol.* 9:109.  
 Ward, J. F. (1988) *Prog. Nucleic Acid Res. Mol. Biol.* 35:95.

## ISOENZYMES

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### Key Words

- Antigenicity** Property of some substances (mostly proteins) to elicit antibodies after introduction into a foreign (other than self) organism.
- Electrophoresis** Technique used to separate charged particles in solution, by the differences in their rates of migration in an applied electric field.
- Epigenetic** Modification of gene products by events or factors that occur after transcription and translation of the gene.
- Fusion Protein** Protein encoded for by a hybrid gene that has fused part of its original coding sequence with coding sequences of another gene for a different protein (e.g., a readily detected marker).
- Locus** Place on a chromosome occupied by a particular gene or its alleles.
- Michaelis Constant** The experimentally determined substrate concentration at which the enzymatic reaction proceeds at half its maximum velocity.
- Ontogenic Development** The course of the development of an organism from fertilization, through maturity, to death.
- Phenotype** The genetically and environmentally determined characteristics of an organism.
- Polymorphism** Occurrence in the same population of two or more alleles at a locus, with at least one allele having a frequency exceeding 1%.
- Translation** The formation of a peptide chain on the mRNA template from individual amino acids.